PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	SETH, Pawan	Examiner:	WANG, Shengjun
Application No.:	09/583,228	Group Art Unit:	1617
Filed:	May 26, 2000	Docket No.:	14577.0023US01
		Confirmation No.:	2041
Title:	SUSTAINED RELEASE VERAPAMIL PHARMACEUTICAL COMPOSITION FREE OF FOOD EFFECT AND A METHOD FOR ALLEVIATING FOOD EFFECT IN DRUG RELEASE		

APPELLANT'S REPLY BRIEF ON APPEAL

Mail Stop Appeal Brief-Patents
Commissioner for Patents
PO Box 1450

Alexandria VA 22313-1450

Dear Sir:

Appellant has received and reviewed the Examiner's Answer mailed on June 3, 2005. Appellant offers the following reply and reserves the right to present further argument at an oral hearing, which Appellant has concurrently requested with the appropriate fee.

Formal Matters

On page 2, item (2) of the Answer, the Examiner indicated that Appellant did not contain a statement identifying the related appeals and interferences. The Appeal Brief on page 3 indicates under the heading: II. Related Appeals and Interferences, the word: "None".

In item (7) of page 2, the Examiner disagrees with Appellant's Grouping of Claims. Appellant has complied with the requirements for such a request and has argued the distinction of the two sets of inventions where one includes a separate intermediate coating over the core. Appellant will rely on the Board's decision on the grouping which has been properly presented.

Substantive Matters

In the last full paragraph of the Examiner's Answer on page 4, the Examiner states that the composition claimed is substantially similar to that taught by Morella et al. (U.S. Patent 5,378,474). He concludes: "The optimization of amount of ingredients to be employed in a composition is considered within the skill of the artisan." Appellant strongly disagrees with this statement. The present invention is not about optimizing amounts of ingredients. It provides an enteric coating with 30-80% of a gastroresistant polymer whereas Morella employs up to 30% of the same polymer. However, the distinction between appellant's claimed invention and the teachings of Morella goes further. Morella teaches a hybrid core coating to achieve different results than the present invention. Morella requires for his composition at least one or two other polymers in the coating in addition to 1-30% enteric polymer. The object of the Morella invention is to provide a slow release of active ingredient at a highly acidic pH and a relatively constant faster rate of release at a less acidic to basic pH over an extended period of time. Col 8, lines 29-33. This is achieved with a hybrid core coating that contains three components: (1) a polymer which is substantially insoluble independent of pH, (2) an enteric polymer which is insoluble in acid pH but partially soluble at a less acidic to basic pH and (3) one component which is at least partially soluble at acidic pH. Alternatively, these components are defined as an insoluble matrix polymer, an enteric polymer, and an acid soluble polymer. Col. 8, lines 38-45. In contrast, the present invention as claimed coats the core with an enteric polymer with the feature of the polymer withstanding the acidic medium of the stomach and duodenum, and as the gastroresistant polymer dissolves, the active ingredient is released in the intestines (less acidic to basic pH). Claim 1 of the present application.

Thus, the present invention is clearly patentably distinct from Morella and not merely an optimization therefrom. Moreover, these features are claimed and distinguishable from the features of the Morella patent. Comparing claim 1 of Morella to Appellant's claim 1 better illustrates this point.

SETH, Pawan Application No. 09/583,228 Claim 1	Morella et al. '474 Claim 1
A tablet composition free of food effect comprising: (a) a core comprising from 20 to 80% by weight of verapamil and from 10 to 80% by weight of a gelling agent; and (b) a coating comprising, based on the weight of the coating, from 30 to 80% of a gastroresistant polymer, and from 10 to 40% of a hydrophilic silicon dioxide, wherein the gastroresistant polymer will dissolve in the intestines while withstanding the acidic medium of the stomach and duodenum, and as the gastroresistant polymer dissolves, verapamil is released in the intestines without the influence of food intake.	A sustained release pharmaceutical pellet composition for administration to a patient at a predetermined dosage and interval which comprises: a core element containing a therapeutically effectively amount of at least one active ingredient having an aqueous solubility of at least 1 in 30 and a coating on said core element which comprises the following components: (a) from 1 to 85% by weight of a matrix polymer which is insoluble at a pH of from 1 to 7.5 and contributes to the control of the rate of release of the active ingredient in the stomach and intestines; (b) from 1 to 30% of an enteric polymer which is substantially insoluble at a pH of from 1 to 4, sufficient to delay the release of the active ingredient in the stomach, but which is soluble at a pH of from 6 to 7.5 so as not to substantially delay release in the intestines: (c) from 1 to 60% of a compound soluble at a pH of from 1 to 4, sufficient to enable initiation of release of the active ingredient in the stomach, said percentages being by weight based on the total weight of components (a), (b), and (c); the ratio of the components (a), (b), and (c) in said coating being such that a dose of the pellet composition delivers to the patient a therapeutically effective amount of said active

	ingredient over the course of said predetermined interval, so as to maintain an active ingredient blood level at steady state of at least 75% of maximum blood level for more than approximately 4 hours and so that the time at which the active ingredient reaches its maximum concentration is between about 4 and about 30 hours.

(Our emphasis added.)

In the last full paragraph of page 4 of the Examiner's Answer, he further states that the composition as claimed is not patentably distinguishable over the prior art, "absent evidence to the contrary". He then starts a sentence but does not complete it: "No such evidence is…". On page 5, the Examiner refers to evidence presented during the prosecution of the present application by Dr. Seth, the inventor. The Examiner criticized the Declaration for two reasons:

1) The Declaration is not commensurate in scope of the claimed invention because of the word "comprising".

To state that the Declaration fails to be commensurate in scope to the claims because of the word "comprising" is confusing at best, especially without further explanation. No explanation is provided in the Examiner's Answer. It is recognized that a Declaration must be commensurate in scope to the claimed invention in order to have probative weight. Appellants respectfully submit that the Declaration of Seth fulfills the requirement. The claimed invention is to a sustained release composition for delivering verapamil to the intestines rather than being released in the stomach and duodenum. The use of the claimed coating, a gastroresistant polymer in an amount of from 30-80 %, over the core provides this feature as demonstrated by Seth in his Declaration. Seth also prepared the same core containing the active ingredient and coated the core with a hybrid core taught by Morella, formulation 3 at column 14. The

dissolution rates were measured at acid pH and at pH 7.5. The dissolution rates at pH 7.5 were found to be markedly different indicating the very feature of the present invention, i.e. rapid release of verapamil at a neutral or higher pH and little or no release in the acid whereas the Morella composition showed a slow release in the acid and a continued steady release but much slower than Seth at the higher pH. Thus the Declaration of Seth is commensurate with the features of the present claimed invention and shows it to be distinct from the Morella composition.

2) The Examiner states: "Appellants' own experiments showing the inferior of the cited references lack probative force".

The Examiner's criticism here is without foundation and blatantly wrong. The Seth Declaration was not presented to show inferior results in the prior art but to show that the Seth invention is distinct from the prior art. The Declaration showed a side-by-side comparison of the dissolution rates at two pH values for Appellant's composition as claimed and Morella's composition. The results speak for themselves and must be given probative weight.

In view of the above, it is respectfully submitted, based on the present facts and applicable law, that Appellant's claimed invention is patentable. It is earnestly requested that the Honorable Board reverse the Examiner's rejection, and that all of the pending claims be allowed.

Please charge any additional fees or credit overpayment to Merchant & Gould Deposit Account No. 13-2725.

Respectfully submitted,

Date: July 20, 2005

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